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(54) Title: NOVEL PEPTIDES

(54) 発明の名称: 新規ペプチド

(57) Abstract: Novel peptides compounds inducing the secretion of growth hormone. Peptide compounds or pharmaceutically acceptable salts thereof having an activity of elevating calcium ion concentration in cells which are characterized in that at least one amino acid has been substituted by a modified amino acid and/or a non-amino acid compound.

(57) 要約:

成長ホルモンの分泌を誘導する新規ペプチド系化合物を提供する。

細胞内のカルシウムイオン濃度を上昇させる活性を有し、少なくとも一つのアミノ酸が修飾アミノ酸及び／又は非アミノ酸化合物により置換されたことを特徴とするペプチド系化合物又はその薬学的に許容される塩。

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Scope of Claims

1. A peptide compound or pharmaceutically acceptable salt thereof with the following characteristics. At least one amino acid of a peptide having activity that increases the calcium ion concentration within a cell undergoes replacement using a modified amino acid and/or a non-amino acid compound.

2. (a) The peptide compound or pharmaceutically acceptable salt thereof described in Section 1 of the scope of claims containing an amino acid sequence which has (a) the amino acid sequence described in sequence 2 or (b) an amino acid sequence that extends from at least the amino terminal up to number 4 through number 10 in the sequence in question and, where at least one amino acid is missing from the section outside the amino acid sequence in question and to which an amino acid sequence has been substituted or added.

3. The peptide compound or pharmaceutically acceptable salt thereof described in Section 2 of the scope of claims having an amino acid sequence selected from a group composed of the amino acid sequences described in sequence numbers 3, 4, 5, 8, 9, 10, 11, 12, 13, 16, 17, 18, 19, 22 and 23.

4. The peptide compound or pharmaceutically acceptable salt thereof described in Section 2 of the scope of claims having an amino acid sequence selected from a group composed of the amino acid sequences described in sequence numbers 25, 26, 29, 30, 31, 32, 34 and 35.

5. A peptide compound or a pharmaceutically acceptable salt thereof with the following characteristics. The activity of the peptide induces the secretion of growth hormone and increases the calcium ion concentration in a cell. In this peptide, (a) the constituent amino acids have either been modified or not and (b) there is at least one amino acid that has undergone substitution using a non-amino acid compound or not.

6. A peptide compound or pharmaceutically acceptable salt thereof with the following characteristics. The peptide compounds described in Sections 1 and 5 of the scope of claims having amino acid sequences described for sequence numbers 27, 28 and 33.

7. The peptide compound or pharmaceutically acceptable salt thereof described in Section 5 of the scope of claims with the following characteristics. It has (a) the amino acid sequence described in sequence number 2 or (b) at least the amino sequence from the amino terminal up to the number four through number ten amino acid sequences. For those sections outside the amino acid sequences from the amino terminal up to the number four through number ten amino acid sequences, it lacks at least one amino acid and contains an amino acid sequence that was substituted and/or added.

8. The peptide compound or pharmaceutically acceptable salt thereof described in Section 7 of the scope of claims with the following characteristics. It has one amino acid sequence selected from the group made up of the amino acid sequences described in sequence numbers 3, 4, 5, 8, 9, 10, 11, 12, 13, 16, 17, 18, 19, 22 and 23.

9. The peptide compound or pharmaceutically acceptable salt thereof described in Section 7 of the scope of claims with the following characteristics. It has one amino acid sequence selected from the group made up of the amino acid sequences described in sequence numbers 25, 26, 29, 30, 31, 32, 34 and 35.

10. A peptide compound or pharmaceutically acceptable salt thereof described in Sections 1 and 5 of the scope of claims, where the section corresponding to the amino acid sequences from the number one of the amino terminal up to number four are expressed using the following formula.

A – B – C – D –

Where A is an amino acid, a non-amino acid compound or is absent, and where B is an amino acid, a non-amino acid compound or is absent. (Note that molecular chain length "A + B" has a length corresponding to the peptide length.)

C and D may be the same or differ and they represent (a) a modified amino acid, (b) an amino acid with a hydrophobic side-chain or (c) an amino acid with a basic side-chain.

11. The peptide compound or pharmaceutically acceptable salt thereof described in Section 10 of the scope of claims with the following characteristics. "C" is either (a) a modified amino acid into which a saturated or unsaturated alkyl chain or chains having carbon numbers of one or more have been introduced into the alpha carbon of the amino acid through ester, ether, thither, amide or disulfide bonds by using or not using alkaline groups having a carbon number of one or more, or (b) a modified amino acid into which a saturated or unsaturated alkyl chain with a carbon number of one or more has been introduced into the alpha carbon of the amino acid through ester, ether, thioether, amide or disulfide bonds by using or not using alkaline groups having a carbon number of one or more.

12. In the single amino acid sequence selected from the group made up of the amino acid sequences described in sequence numbers 2, 3, 9, 10, 11, 16, 17, 22, 25, 26, 27, 28, 29, 30 and 31, the section corresponding to the amino acid sequence from the amino terminal up to number one through number four is the peptide compound or pharmaceutically acceptable salt thereof which is the peptide compound described in Sections 10 or 11 of the scope of claims.

13. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 3, 5, 7 or 8 of the scope of claims, in which the modified amino acid is the third amino acid from the amino terminal.

14. The peptide compound or pharmaceutically acceptable salt thereof described in Section 13 of the scope of claims with the following characteristics. The amino acid in the modified amino acid is either serine or cysteine.

15. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 3, 5, 7 or 8 of the scope of claims, which contains a modified amino acid into which either (a) a saturated or unsaturated alkyl chain or chains having carbon numbers of one or more have been introduced into the alpha carbon of the amino acid through ester, ether, thioester, thioether, amide or carbamide bonds by using or not using alkylene groups having a carbon number of one or more, or (b) a modified amino acid into which a saturated or unsaturated alkyl chain with a carbon number of one or more or H has been introduced.

16. The amino acid into which the modified amino acid that is introduced to the alpha carbon of the amino acid is either (a) the saturated or unsaturated alkyl chain or chains having a carbon number of one through ester, ether, thioester, thioether, disulfide, amide, carbamide or thiocarbamide bonds either using or not using alkylene groups with a carbon number of one or more, or (b) the amino acid into which saturated or unsaturated alkyl chains having carbon numbers of one or more are introduced, which are the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1, 2, 4, 5, 6, 7 9, 10 or 12.

17. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 3, 5, 7 or 8 of the scope of claims that has a modified amino acid that has been modified by ester bonding.

18. The peptide compound or pharmaceutically acceptable salt thereof described in Sections 1, 2, 4, 5, 6, 7, 9, 10, 11 or 12 of the scope of claims, which contains a modified amino acid that was modified when the functional group of the side-chains of the amino acid formed ester bonds.

19. The peptide compound or pharmaceutically acceptable salt thereof described in Section 17 of the scope of claims, which has an amino acid in which the fatty acid has undergone an ester bond to the hydroxyl group of the side-chains of the amino acid.

20. The peptide compound or pharmaceutically acceptable salt thereof described in Section 18 of the scope of claims, which has an amino acid in which the fatty acid has undergone thioester bonding to the mercapto group or ester bonding to the hydroxyl group of the side-chains of the amino acid.

21. The peptide compound or pharmaceutically acceptable salt thereof described in Section 19 of the scope of claims, which has an amino acid in which bonded fatty acid has a carbon number from 2 to 35.

22. The peptide compound or pharmaceutically acceptable salt thereof described in Section 20 of the scope of claims, in which the fatty acid has a carbon number from 2 to 35.

23. The peptide compound or pharmaceutically acceptable salt thereof described in Section 21 of the scope of claims, which has

an amino acid in which the bonded fatty acid is selected from a group of fatty acids having carbon numbers of 2, 4, 6, 8, [redacted]2, 14, 16 and 18.

24. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 22 of the scope of claims, which is a fatty acid selected from a group composed of the fatty acids having carbon numbers of 2, 4, 6, 8, 10, 12, 14, 16 and 18.

25. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 23 of the scope of claims in which the bonded fatty acid is an octanoic acid, its monoen fatty acid, or its polyen fatty acid.

26. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 24 of the scope of claims in which the fatty acid is an octanoic acid, its monoen fatty acid, or its polyen fatty acid.

27. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 23 of the scope of claims in which the bonded fatty acid is a decanoic acid, its monoen fatty acid, or its polyen fatty acid.

28. The peptide compound or a pharmaceutically acceptable salt thereof described in Section 24 of the scope of claims in which the fatty acid is a decanoic acid, its monoen fatty acid, or its polyen fatty acid.

29. A peptide compound with the following characteristics. Additional basic amino acids bond to the carboxyl terminal of the peptide compounds described in Sections 1 through 28 of the scope of claims.

30. The peptide compounds described in Sections 1, 2, 3, 5, 7, 8, 13, 14, 15, 17, 19, 21, 23, 25 and 27 of the scope of claims with the following characteristics. The amino terminal is modified using a saturated or unsaturated alkyl or acyl group with a carbon number of one or more and/or, the OH of the carboxyl group at the carboxyl terminal is OZ or NR2R3 (where Z is a pharmaceutically acceptable positive ion or a low-

grade branching chain or a non-branching chain alkyl group, and R2 and R3 are selected from a group made up of H and [redacted]grade branching chains or non-branching ch[redacted]alkyl groups, which may indicate groups identical to or different from each other).

31. The peptide compounds described in Sections 1, 2, 4, 5, 6, 7, 9, 10, 11, 12, 16, 18, 20, 22, 24, 26, 28 or 29 of the scope of claims with the following characteristics. The amino terminal amino group is modified by introducing a saturated or unsaturated alkyl or acyl group with a carbon number of one or more and/or, the OH of the carboxyl group at the carboxyl terminal is OZ or NR2R3 (where Z is a pharmaceutically acceptable positive ion or a low-grade branching chain or a non-branching chain alkyl group, and R2 and R3 are selected from a groups made up of H and low-grade branching chains or non-branching chain alkyl groups, which may indicate groups identical to or different from each other).

32. A peptide compound with the following characteristics. An additional basic group has been introduced to the amide inducer of the carboxyl terminal of the peptide compounds described in Sections 30 and 31 of the scope of claims.

33. A pharmaceutical compound having as its active ingredient the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1 through 32 of the scope of claims.

34. A pharmaceutical compound for the purpose of treating illnesses caused by a deficiency of or a decrease in growth hormone having, as its effective ingredient the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1 through 32 of the scope of claims.

35. A pharmaceutical compound for the purpose of treating illnesses not caused by a deficiency of or a decrease in growth hormones, containing the peptide compounds or pharmaceutically acceptable salts thereof described in Sections 1 through 32 of the scope of claims and a treatment agent pertaining to illnesses not caused by a deficiency of or a decrease in growth hormone.

36. The pharmaceutical compound described in Sections 33 through 35 of the scope of claims for the purpose of applications on non-human animals.

37. A method of treating illnesses caused by a deficiency of or a decrease in growth hormones involving

the administration of pharmaceutical compounds, the active ingredient of which is a peptide compound described in Sections 1 through 32 of the scope of claims or the pharmaceutically acceptable salts thereof.

38. An agent for treating illnesses not caused by a deficiency of or a decrease in growth hormone and a method of treating illnesses not caused by a deficiency of or a decrease in growth hormone involving the administration of pharmaceutical compounds containing a peptide compound or the pharmaceutically acceptable salts thereof, described in Sections 1 through 32 of the scope of claims.

39. Methods of treatment described in Sections 37 and 38 of the scope of claims for applications on non-human animals.

40. DNA that is encoded with amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims, where the amino acid sequences coded into said DNA contain DNA that has basic sequences encoding peptides containing recognized sequences for which at least one amino acid is modifiable.

41. The DNA described in Section 40 of the scope of claims where one of the basic sequences is selected from a group made up of the basic sequences described in sequence numbers 6, 7, 14, 15, 20, 21, 24, 36, 37, 38, and 39.

42. The DNA described in Section 40 of the scope of claims where one of the basic sequences is selected from a group made up of the basic sequences described in sequence numbers 6, 7, 14, 15, 20, 21, 24, 36, 37, 38, and 39 and is a basic sequence encoded with amino acid.

43. A vector having the DNA described in Sections 40 through 42 of the scope of claims.

44. A cell containing the vector described in Section 43 of the scope of claims.

45. A cell capable of producing a peptide with at least one amino acid modified in the amino acid sequence, which is a peptide compound with a vector containing the DNA described in Sections 40 through 42 of the scope of claims as well as the amino acid sequence encoded in said DNA.

46. An antibody for the peptide compounds described in Sections 1 through 32 of the scope of claims.

47. A method of assaying the peptide compounds described in Sections 1 through 32 of the scope of claims with the following characteristics. The antibody described in Section 46 of the scope of claims is used to detect the peptide compounds described in Sections 1 through 32 of the scope of claims.

48. A detection kit for the peptide compounds described in Sections 1 through 32 of the scope of claims with the following characteristics. The antibody described in Section 46 of the scope of claims is used to detect the peptide compounds described in Sections 1 through 32 of the scope of claims.

49. A method of manufacturing the peptide compounds described in Sections 1 through 32 of the scope of claims consisting of collecting the desired peptide compounds from cell cultures that have undergone phenotypic transformations. In this manufacturing method, genetic manipulation is used on the peptide compounds described in Sections 1 through 32 of the scope of claims and host cells capable of modifying the side-chains of at least one amino acid in the peptide are transformed phenotypically using a vector containing the DNA described in Sections 40 through 42 of the scope of claims.

50. A method of manufacturing the peptide compounds described in Sections 1 through 32 of the scope of claims with the following characteristics. After collecting the desired substances from cell cultures that have been phenotypically transformed, select amino acids are modified chemically. In this manufacturing method, genetic manipulation is used on the peptide compounds described in Sections 1 through 32 of the scope of claims and host cells capable of modifying the side-chains of at least one amino acid in the peptide are transformed phenotypically using a vector containing the DNA described in Sections 40 through 42 of the scope of claims.

51. A method of manufacturing the peptide compounds described in Sections 19 through 28 of the scope of claims with the following characteristics. In the method of manufacturing the peptide compounds described in Sections 19 through 28 using genetic manipulation, cells are used which have activity that causes the fatty acids to undergo ester bonding with the hydroxyl groups of the side-chains of the amino acids or to undergo thioester bonding with the mercapto groups.

52. A method of manufacturing the peptide compounds described in Sections 19 through 28 of the scope of claims with the following characteristics. Cells are used having serine-acyl activity that cause fatty acids to

undergo ester bonding with the hydroxyl groups of the side-chains of the serine in the amino acid sequences described in [redacted]ence number 8.

53. A method of manufacturing the peptide compounds described in Sections 19 through 28 of the scope of claims with the following characteristics. Cells are used having acyl activity that cause the fatty acid to undergo ester bonding with the hydroxyl groups of the side-chains of the threonine in the amino acid sequence described in sequence number 28.

54. A pharmaceutical compound for the genetic treatment of illnesses caused by a decrease in or lack of growth hormone that works by manifesting peptides having at least one modified amino acid that has activity that increases the calcium ion concentration in the cell. This is accomplished by integrating a vector containing DNA that encodes the amino acid sequence of the peptide compounds described in Sections 1 through 32 of the scope of claims into the cell of the organism.

55. A method of treating illnesses caused by a decrease in or lack of growth hormone with the following characteristics. Peptides having activity that induces the secretion of growth hormones are manifested by integrating vectors containing the DNA that encodes the amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims into the cells of the organism. The peptides containing the amino acid sequences encoded in said DNA are produced as peptides having recognized sequences in which at least one of the amino acids can be modified.

56. A pharmaceutical compound for the genetic treatment of illnesses that are not caused by a decrease in or lack of growth hormone. This is accomplished by integrating vectors containing DNA in which the amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims are encoded into the cells of the organism. These have activity which increases the concentration of the calcium ions in the cells and peptides are manifested that have at least one modified amino acid.

57. A method of treati[redacted]nesses not caused by a decrease in or lack [redacted]owth hormone with the following characteristics. Vectors containing the DNA that encodes the amino acid sequences of the peptide compounds described in Sections 1 through 32 of the scope of claims are integrated into the cells of an organism capable of producing as peptides, peptides having recognized sequences with at least one modifiable amino acid in the amino acid sequence in question. This allows the expression of peptides having activity that induces the secretion of growth hormone.

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<213> Rattus norvegicus
<223> Amino acid sequence for rat endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 10
Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Ala Gln Arg Lys Glu
1 5 10 15
Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg
20 25

<210> 11
<211> 27
<212> PRT
<213> Homo sapiens
<223> Amino acid sequence for human endogenous peptides (27 amino acids)of growth hormone secretagogue
<400> 11
Gly Ser Ser Phe Leu Ser Pro Glu His Gln Arg Val Gln Arg Lys Glu
1 5 10 15
Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg
20 25

<210> 12
<211> 116

<212> PRT
<213> Rattus norvegicus
<223> Amino acid sequence for a prepro-form of rat endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 12

Met Val Ser Ser Ala Thr Ile Cys Ser Leu Leu Leu Leu Ser Met Leu
1 5 10 15
Trp Met Asp Met Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His
20 25 30
Gln Lys Ala Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln
35 40 45
Pro Arg Ala Leu Glu Gly Trp Leu His Pro Glu Asp Arg Gly Gln Ala
50 55 60
Glu Glu Ala Glu Glu Glu Leu Glu Ile Arg Phe Asn Ala Pro Phe Asp
65 70 75 80
Val Gly Ile Lys Leu Ser Gly Ala Gln Tyr Gln Gln His Gly Arg Ala
85 90 95
Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Val Lys Glu Ala
100 105 110
Pro Ala Asn Lys
115

<210> 13
<211> 116
<212> PRT
<213> Homo sapiens
<223> Amino acid sequence for prepro-form of human endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 13

Met Pro Ser Pro Gly Thr Val Cys Ser Leu Leu Leu Leu Gly Met Leu
1 5 10 15
Trp Leu Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His
20 25 30
Gln Arg Val Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln
35 40 45
Pro Arg Ala Leu Ala Gly Trp Leu Arg Pro Glu Asp Gly Gly Gln Ala

50 55 60
Glu Gly Ala Glu Asp Glu Leu Glu Val Arg Phe Asn Ala Pro Phe Asp
65 70 75 80
Val Gly Ile Lys Leu Ser Gly Val Gln Tyr Gln Gln His Ser Gln Ala
85 90 95
Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Ala Lys Glu Ala
100 105 110
Pro Ala Asp Lys
115

<210> 14
<211> 498
<212> cDNA
<213> Rattus norvegicus
<220>
<221> CDS
<222> (31)... (378)
<223> Base sequence of cDNA coding prepro-form of rat endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 14

tccagatcat ctgtcctcac caccaaggcc atg gtg tct tca gcg act 48
Met Val Ser Ser Ala Thr
1 5

atc tgc agt ttg cta ctc ctc agc atg ctc tgg atg gac atg gcc atg 96
Ile Cys Ser Leu Leu Leu Leu Ser Met Leu Trp Met Asp Met Ala Met
10 15 20

gca ggt tcc agc ttc ttg agc cca gag cac cag aaa gcc cag aga aag 144
Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Ala Gln Arg Lys
25 30 35

gaa tcc aag aag cca cca gct aaa ctg cag cca cga gct ctg gaa ggc 192
Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg Ala Leu Glu Gly
40 45 50

tgg ctc cac cca gag gac aga gga caa gca gaa gag gca gag gag gag 240
Trp Leu His Pro Glu Asp Arg Gly Gln Ala Glu Glu Ala Glu Glu Glu
55 60 65 70

ctg gaa atc agg ttc aat gct ccc ttc gat gtt ggc atc aag ctg tca 288

Leu Glu Ile Arg Phe Asn Ala Pro Phe Asp Val Gly Ile Lys Leu Ser
75 80 85
gga gct cag tac cag cag cat ggc cgg gcc ctg gga aag ttt ctt cag 336
Gly Ala Gln Tyr Gln Gln His Gly Arg Ala Leu Gly Lys Phe Leu Gln
90 95 100
gat atc ctc tgg gaa gag gtc aaa gag gcg cca gct aac aag 378
Asp Ile Leu Trp Glu Glu Val Lys Glu Ala Pro Ala Asn Lys
105 110 115
taaccactga caggactggt ccctgtactt tcctcctaag caagaactca catccagctt 438
ctgcctcctc tgcaactccc agcactctcc tgctgactta caaataaatg ttcaagctgt 498

<210> 15
<211> 508
<212> DNA
<220>
<221> CDS
<222> (34)... (381)
<213> Homo sapiens
<223> Base sequence of cDNA coding prepro-form of human endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 15
gcaggcccac ctgtctgcaa cccagctgag gcc atg ccc tcc cca 45
Met Pro Ser Pro
1
ggg acc gtc tgc agc ctc ctg ctc ctc ggc atg ctc tgg ctg gac ttg 93
Gly Thr Val Cys Ser Leu Leu Leu Leu Gly Met Leu Trp Leu Asp Leu
5 10 15 20
gcc atg gca ggc tcc agc ttc ctg agc cct gaa cac cag aga gtc cag 141
Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Arg Val Gln
25 30 35
aga aag gag tcg aag aag cca cca gcc aag ctg cag ccc cga gct cta 189
Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg Ala Leu
40 45 50
gca ggc tgg ctc cgc ccg gaa gat gga ggt caa gca gaa ggg gca gag 237
Ala Gly Trp Leu Arg Pro Glu Asp Gly Gly Gln Ala Glu Gly Ala Glu
55 60 65

gat gaa ctg gaa gtc cgg ttc aac gcc ccc ttt gat gtt gga atc aag 285
Asp Glu Leu Glu Val Arg Phe Asn Ala Pro Phe Asp Val Gly Ile Lys
70 75 80
ctg tca ggg gtt cag tac cag cag cac agc cag gcc ctg ggg aag ttt 333
Leu Ser Gly Val Gln Tyr Gln Gln His Ser Gln Ala Leu Gly Lys Phe
85 90 95 100
ctt cag gac atc ctc tgg gaa gag gcc aaa gag gcc cca gcc gac aag 381
Leu Gln Asp Ile Leu Trp Glu Glu Ala Lys Glu Ala Pro Ala Asp Lys
105 110 115
tgatcgccca caagccttac tcacctctct ctaagtttag aagcgctcat 431

ctggcttttc gcttgcttct gcagcaactc ccacgactgt tgtacaagct caggaggcga 491
ataaatgttc aaactgt 508

<210> 16
<211> 28
<212> PRT
<213> Sus scrofa (pig)
<223> Amino acid sequence for porcine endogenous peptides of growth hormone secretagogue
<400> 16
Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Val Gln Gln Arg Lys
1 5 10 15
Glu Ser Lys Lys Pro Ala Ala Lys Leu Lys Pro Arg
20 25

<210> 17
<211> 27
<212> PRT
<213> Sus scrofa (pig)
<223> Amino acid sequence for porcine endogenous peptides (27 amino acids) of growth hormone secretagogue
<400>17
Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Val Gln Arg Lys Glu
1 5 10 15
Ser Lys Lys Pro Ala Ala Lys Leu Lys Pro Arg

20 25

<210> 18
<211> 118
<212> PRT
<213> Sus scrofa (pig)
<223> Amino acid sequence for prepro-form of porcine endogenous peptides of growth hormone secretagogue
<400> 18

Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Leu Ser Val Leu
1 5 10 15
Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu
20 25 30
His Gln Lys Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Ala Ala Lys
35 40 45
Leu Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu Asp Ser Gly
50 55 60
Glu Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe Asn Ala Pro
65 70 75 80
Cys Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp Gln His Gly
85 90 95
Gln Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Val Thr
100 105 110
Glu Ala Pro Ala Asp Lys
115

<210> 19
<211> 117
<212> PRT
<213> Sus scrofa (pig)
<223> Amino acid sequence for prepro-form of porcine endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 19

Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Leu Ser Val Leu
1 5 10 15
Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu

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            20                  25                  30
His Gln Lys Val Gln Arg Lys Glu Ser Lys Lys Pro Ala Ala Lys Leu
        35                  40                  45
Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu Asp Ser Gly Glu
    50                  55                  60
Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe Asn Ala Pro Cys
65                  70                  75                  80
Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp Gln His Gly Gln
                85                  90                  95
Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu Val Thr Glu
            100                 105                 110
Ala Pro Ala Asp Lys
        115
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<210> 20
<211> 494
<212> DNA
<220>
<221> CDS
<222> (9)... (362)
<213> Sus scrofa (pig)
<223> Base sequence of cDNA coding prepro-form of porcine endogenous peptides of growth hormone secretagogue
<400> 20

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ctgaggcc atg ccc tcc acg ggg acc att tgc agc ctg ctg ctc ctc        47
        Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Leu
          1               5                  10
agc gtg ctc ctc atg gca gac ttg gcc atg gcg ggc tcc agc ttc ttg      95
Ser Val Leu Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu
    15                  20                  25
agc ccc gaa cac cag aaa gtg cag cag aga aag gag tcc aag aag cca     143
Ser Pro Glu His Gln Lys Val Gln Gln Arg Lys Glu Ser Lys Lys Pro
30                  35                  40                  45
gca gcc aaa ctg aag ccc cgg gcc ctg gaa ggc tgg ctc ggc cca gaa     191
Ala Ala Lys Leu Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu
                50                  55                  60
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gac agt ggt gag gtg gaa ggc acg gag gac aag ctg gaa atc cgg ttc 239
Asp Ser Gly Glu Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe
65 70 75

aac gcc ccc tgt gat gtt ggg atc aag ttg tca ggg gct cag tcc gac 287
Asn Ala Pro Cys Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp
80 85 90

cag cac ggc cag ccc ctg ggg aaa ttt ctc cag gac atc ctc tgg gaa 335
Gln His Gly Gln Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu
95 100 105

gag gtc act gag gcc ccg gcc gac aag tgattgtccc tgagaccagc 382
Glu Val Thr Glu Ala Pro Ala Asp Lys
110 115

cacctctgtt ctcccagcct cctaagggct cacctggctt ccaggacgct tccactatca 442

cacccagctc tgagggatgc tagcctggga ggtgaataaa cattcagact gg 494

<210> 21
<211> 491
<212> DNA
<220>
<221> CDS
<222> (9)... (359)
<213> Sus scrofa (pig)
<223> Base sequence of cDNA coding prepro-form of porcine endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 21

ctgaggcc atg ccc tcc acg ggg acc att tgc agc ctg ctg ctc ctc 47
Met Pro Ser Thr Gly Thr Ile Cys Ser Leu Leu Leu Leu
1 5 10

agc gtg ctc ctc atg gca gac ttg gcc atg gcg ggc tcc agc ttc ttg 95
Ser Val Leu Leu Met Ala Asp Leu Ala Met Ala Gly Ser Ser Phe Leu
15 20 25

agc ccc gaa cac cag aaa gtg cag aga aag gag tcc aag aag cca gca 143
Ser Pro Glu His Gln Lys Val Gln Arg Lys Glu Ser Lys Lys Pro Ala
30 35 40 45

gcc aaa ctg aag ccc cgg gcc ctg gaa ggc tgg ctc ggc cca gaa gac 191

Ala Lys Leu Lys Pro Arg Ala Leu Glu Gly Trp Leu Gly Pro Glu Asp
50 55 60
agt ggt gag gtg gaa ggc acg gag gac aag ctg gaa atc cgg ttc aac 239
Ser Gly Glu Val Glu Gly Thr Glu Asp Lys Leu Glu Ile Arg Phe Asn
65 70 75
gcc ccc tgt gat gtt ggg atc aag ttg tca ggg gct cag tcc gac cag 287
Ala Pro Cys Asp Val Gly Ile Lys Leu Ser Gly Ala Gln Ser Asp Gln
80 85 90
cac ggc cag ccc ctg ggg aaa ttt ctc cag gac atc ctc tgg gaa gag 335
His Gly Gln Pro Leu Gly Lys Phe Leu Gln Asp Ile Leu Trp Glu Glu
95 100 105
gtc act gag gcc ccg gcc gac aag tgattgtccc tgagaccagc 379
Val Thr Glu Ala Pro Ala Asp Lys
110 115

cacctctgtt ctcccagcct cctaagggct cacctggctt ccaggacgct tccactatca 439
cacccagctc tgagggatgc tagcctggga ggtgaataaa cattcagact gg 491

<210> 22
<211> 27
<212> PRT
<213> Bos taurus
<223> Amino acid sequence for bovine endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 22
Gly Ser Ser Phe Leu Ser Pro Glu His Gln Glu Leu Gln Arg Lys Glu
1 5 10 15
Ala Lys Lys Pro Ser Gly Arg Leu Lys Pro Arg
20 25

<210> 23
<211> 89
<212> PRT
<213> Bos taurus
<223> Partial amino acid sequence for a prepro-form of bovine endogenous peptides (27 amino acids) of growth hormone secretagogue

<400> 23

Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Glu
1 5 10 15
Leu Gln Arg Lys Glu Ala Lys Lys Pro Ser Gly Arg Leu Lys Pro Arg
20 25 30
Thr Leu Glu Gly Gln Phe Asp Phe Glu Val Gly Ser Gln Ala Glu Gly
35 40 45
Ala Glu Asp Glu Leu Glu Ile Arg Phe Asn Ala Phe Phe Asn Ile Gly
50 55 60
Ile Lys Leu Ala Gly Ala Gln Ser Leu Gln His Gly Gln Thr Leu Gly
65 70 75 80
Lys Phe Leu Gln Asp Ile Leu Trp Glu
85

<210> 24
<211> 267
<212> DNA
<220>
<221> CDS
<222> (1)... (267)
<213> Bos taurus
<223> Base sequence of cDNA coding prepro-form of bovine endogenous peptides (27 amino acids) of growth hormone secretagogue
<400> 24

gac ttg gcc atg gcg ggc tcc agc ttt ctg agc ccc gaa cat cag gaa 48
Asp Leu Ala Met Ala Gly Ser Ser Phe Leu Ser Pro Glu His Gln Glu
1 5 10 15
ctg cag aga aag gaa gct aag aag cca tca ggc aga ctg aag ccc cgg 96
Leu Gln Arg Lys Glu Ala Lys Lys Pro Ser Gly Arg Leu Lys Pro Arg
20 25 30
acc ctg gaa ggc cag ttt gac ccg gag gtg gga agt cag gcg gaa ggt 144
Thr Leu Glu Gly Gln Phe Asp Phe Glu Val Gly Ser Gln Ala Glu Gly
35 40 45
gca gag gac gag ctg gaa atc cgg ttc aac gcc ccc ttt aac att ggg 192
Ala Glu Asp Glu Leu Glu Ile Arg Phe Asn Ala Phe Phe Asn Ile Gly
50 55 60

atc aag cta gca ggg gct cag tcc ctc cag cat ggc cag acg ttg ggg 240
Ile Lys Leu Ala Gly Ala Gln Ser Leu Gln His Gly Gln Thr Leu Gly
65 70 75 80
aag ttt ctt cag gac atc ctc tgg gaa 267
Lys Phe Leu Gln Asp Ile Leu Trp Glu
85

<210> 25
<211> 24
<212> PRT
<213> Gallus domesticus
<223> Amino acid sequence for chicken endogenous peptides of growth hormone secretagogue
<400> 25
Gly Ser Ser Phe Leu Ser Pro Thr Tyr Lys Asn Ile Gln Gln Gln Lys
1 5 10 15
Gly Thr Arg Lys Pro Thr Ala Arg
20

<210> 26
<211> 21
<212> PRT
<213> Anguilla japonica
<220>
<221> AMIDATION
<222> 21
<223> Amino acid sequence for eel endogenous peptides of growth hormone secretagogue
<400> 26
Gly Ser Ser Phe Leu Ser Pro Ser Gln Arg Pro Gln Gly Lys Asp Lys
1 5 10 15
Lys Pro Pro Arg Val
20

<210> 27
<211> 28

<212> PRT
<213> Rana cafesbeiana
<223> Amino acid sequence for frog endogenous peptides of growth hormone secretagogue
<400> 27

Gly Leu Ser Phe Leu Ser Pro Ala Glu Met Gln Lys Ile Ala Glu Arg
1 5 10 15
Gln Ser Gln Asn Lys Leu Arg His Gly Asn Met Arg
20 25

<210> 28
<211> 27
<212> PRT
<213> Xenopus laevis
<223> Amino acid sequence for frog (Xenopus laevis) endogenous peptides of growth hormone secretagogue
<400> 28

Gly Leu Thr Phe Leu Ser Pro Ala Asp Met Gln Lys Ile Ala Glu Arg
1 5 10 15
Gln Ser Gln Asn Lys Leu Arg His Gly Asn Met
20 25

<210> 29
<211> 23
<212> PRT
<213> Oncorhynchus mykiss
<220>
<221>AMIDATION
<222> 23
<223> Amino acid sequence for rainbow trout endogenous peptides (23 amino acids) of growth hormone secretagogue
<400> 29

Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Val Arg Gln Gly
1 5 10 15
Lys Gly Lys Pro Pro Arg Val
20

<210> 30
<211> 20
<212> PRT
<213> Oncorhynchus mykiss
<220>
<221> AMIDATION
<222> 20
<223> Amino acid sequence for rainbow trout endogenous peptides (20 amino acids) of growth hormone secretagogue
<400> 30
Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Gly Lys Gly Lys
1 5 10 15
Pro Pro Arg Val
20

<210> 31
<211> 28
<212> PRT
<213> Canis familiaris
<223> Amino acid sequence for dog endogenous peptides of growth hormone secretagogue
<400> 31
Gly Ser Ser Phe Leu Ser Pro Glu His Gln Lys Leu Gln Gln Arg Lys
1 5 10 15
Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg
20 25

<210> 32
<211> 108
<212> PRT
<213> Anguilla japonica
<223> Amino acid sequence for prepro-form of eel endogenous peptides of growth hormone secretagogue
<400> 32
Met Lys Arg Thr Ala Tyr Ile Ile Leu Leu Val Cys Val Leu Ala Leu

1 5 10 15
Trp Met Asp Ser Val Gln Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln
20 25 30
Arg Pro Gln Gly Lys Asp Lys Lys Pro Pro Arg Val Gly Arg Arg Asp
35 40 45
Ser Asp Gly Ile Leu Asp Leu Phe Met Arg Pro Pro Leu Gln Asp Glu
50 55 60
Asp Ile Arg His Ile Thr Phe Asn Thr Pro Phe Glu Ile Gly Ile Thr
65 70 75 80
Met Thr Glu Glu Leu Phe Gln Gln Tyr Gly Glu Val Met Gln Lys Ile
85 90 95
Met Gln Asp Leu Leu Met Asp Thr Pro Ala Lys Glu
100 105

<210> 33
<211> 114
<212> PRT
<213> Xenopus laevis
<223> Amino acid sequence frog (Xenopus laevis) endogenous peptides of growth hormone secretagogue
<400>33
Met Asn Phe Gly Lys Ala Ala Ile Phe Gly Val Val Leu Phe Cys Leu
1 5 10 15
Leu Trp Thr Glu Gly Ala Gln Ala Gly Leu Thr Phe Leu Ser Pro Ala
20 25 30
Asp Met Gln Lys Ile Ala Glu Arg Gln Ser Gln Asn Lys Leu Arg His
35 40 45
Gly Asn Met Asn Arg Arg Gly Val Glu Asp Asp Leu Ala Gly Glu Glu
50 55 60
Ile Gly Val Thr Phe Pro Leu Asp Met Lys Met Thr Gln Glu Gln Phe
65 70 75 80
Gln Lys Gln Arg Ala Ala Val Gln Asp Phe Leu Tyr Ser Ser Leu Leu
85 90 95
Ser Leu Gly Ser Val Gln Asp Thr Glu Asp Lys Asn Glu Asn Pro Gln
100 105 110
Ser Gln

<210> 34
<211> 82
<212> PRT
<213> Oncorhynchus mykiss
<223> Amino acid sequence for prepro-form of rainbow trout endogenous peptides (23 amino acids) of growth hormone secretagogue
<400>34

Met Ile Leu Met Leu Cys Thr Leu Ala Leu Trp Ala Lys Ser Val Ser
1 5 10 15
Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Val Arg Gln
20 25 30
Gly Lys Gly Lys Pro Pro Arg Val Gly Arg Arg Asp Ile Glu Ser Phe
35 40 45
Ala Glu Leu Phe Glu Gly Pro Leu His Gln Glu Asp Lys His Asn Thr
50 55 60
Ile Lys Ala Pro Phe Glu Met Gly Ile Thr Met Ser Glu Glu Glu Phe
65 70 75 80
Gln Glu

<210> 35
<211> 99
<212> PRT
<213> Oncorhynchus mykiss
<223> Amino acid sequence for prepro-form of rainbow trout endogenous peptides (20 amino acids) of growth hormone secretagogue
<400>35

Met Ile Leu Met Leu Cys Thr Leu Ala Leu Trp Ala Lys Ser Val Ser
1 5 10 15
Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro Gln Gly Lys Gly
20 25 30
Lys Pro Pro Arg Val Gly Arg Arg Asp Ile Glu Ser Phe Ala Glu Leu
35 40 45
Phe Glu Gly Pro Leu His Gln Glu Asp Lys His Asn Thr Ile Lys Ala
50 55 60
Pro Phe Glu Met Gly Ile Thr Met Ser Glu Glu Glu Phe Gln Glu Tyr

65 70 75 80
Gly Ala Val Leu Gln Lys Ile Leu Gln Asp Val Leu Gly Asp Thr Ala
85 90 95
Thr Ala Glu

<210> 36
<211> 503
<212> DNA
<220>
<221> CDS
<222> (66)... (389)
<213> Anguilla japonica
<223> Base sequence of cDNA coding prepro-form of eel endogenous peptides of growth hormone secretagogue
<400> 36
tccaagaggc actgggtttc ctcttaaagt gcaaaactcc actgtgagct tcagacatga 60

ggcag atg aaa cgc acc gca tac atc atc ctg ctg gtc tgc gtc ctg 107
Met Lys Arg Thr Ala Tyr Ile Ile Leu Leu Val Cys Val Leu
1 5 10
gcg ctg tgg atg gac tct gtc cag gct ggc tcc agc ttc ctc agc ccc 155
Ala Leu Trp Met Asp Ser Val Gln Ala Gly Ser Ser Phe Leu Ser Pro
15 20 25 30
tca cag aga ccg cag ggg aag gat aag aag cct ccc agg gtt ggc aga 203
Ser Gln Arg Pro Gln Gly Lys Asp Lys Lys Pro Pro Arg Val Gly Arg
35 40 45
cga gac tca gat ggg atc ctg gac ctg ttt atg agg ccc cca ttg cag 251
Arg Asp Ser Asp Gly Ile Leu Asp Leu Phe Met Arg Pro Pro Leu Gln
50 55 60
gat gaa gac atc aga cac att acg ttt aac act cct ttt gag atc ggg 299
Asp Glu Asp Ile Arg His Ile Thr Phe Asn Thr Pro Phe Glu Ile Gly
65 70 75
atc acc atg act gag gag ctg ttc cag caa tat gga gaa gtg atg cag 347
Ile Thr Met Thr Glu Glu Leu Phe Gln Gln Tyr Gly Glu Val Met Gln
80 85 90
aag atc atg cag gat ttg ctg atg gac aca cct gcc aaa gag 389

Lys Ile Met Gln Asp Leu Leu Met Asp Thr Pro Ala Lys Glu
95 100 105

tgacaagagt ggatatgatc tggacttcat aaaaccctgc gtcccatata ttcctgcatt 449
attgcatgca taattcaacc aattgttaaa catttaataa aattttgcaa acgc 503

<210> 37
<211> 484
<212> DNA
<220>
<221> CDS
<222> (47)... (388)
<213> Xenopus laevis
<223> Base sequence of cDNA coding prepro-form of frog (Xenopus laevis) endogenous peptides of growth hormone secretagogue
<400> 37
tttcacttttt atctcgcagg cggcaccggt gaccaggacc ttcagg 46

atg aat ttt ggt aaa gcc gcc atc ttt ggg gtt gtc ttg ttc tgc ctg 94
Met Asn Phe Gly Lys Ala Ala Ile Phe Gly Val Val Leu Phe Cys Leu
1 5 10 15
ctg tgg acg gag ggg gcc cag gct ggc ttg acc ttc ctg agt cca gcc 142
Leu Trp Thr Glu Gly Ala Gln Ala Gly Leu Thr Phe Leu Ser Pro Ala
20 25 30
gac atg cag aag att gcg gag agg caa tca cag aat aag ctg aga cac 190
Asp Met Gln Lys Ile Ala Glu Arg Gln Ser Gln Asn Lys Leu Arg His
35 40 45
ggc aat atg aat cgc agg ggt gtg gag gat gac ctg gcc ggg gag gag 238
Gly Asn Met Asn Arg Arg Gly Val Glu Asp Asp Leu Ala Gly Glu Glu
50 55 60
atc ggg gtg acc ttc cct ctg gat atg aag atg acg cag gag cag ttc 286
Ile Gly Val Thr Phe Pro Leu Asp Met Lys Met Thr Gln Glu Gln Phe
65 70 75 80
cag aag cag agg gct gcg gtg cag gac ttc ctg tac tcc tcc ctc ctc 334
Gln Lys Gln Arg Ala Ala Val Gln Asp Phe Leu Tyr Ser Ser Leu Leu
85 90 95

tct ctc ggg tca gtg cag gat aca gaa gac aag aat gaa aat cct cag 382
Ser Leu Gly Ser Val Gln Asp Thr Glu Asp Lys Asn Glu Asn Pro Gln
100 105 110
agc caa tgagaatgat gaaaatccgc tcgtctctga tgcccctccc cgatctgtgt 438
Ser Gln

gtctttatta tctctgtgta acccagaaat aaatcttatt tatggc 484

<210> 38
<211> 462
<212> DNA
<220>
<221> CDS
<222> (12)... (257)
<213> Oncorhynchus mykiss
<223> Base sequence of cDNA coding prepro-form of rainbow trout endogenous peptides (23 amino acids) of growth hormone secretagogue
<400> 38
tcacaggtct c atg ata ctg atg ctg tgt act ctg gct ctg tgg gcc 47
Met Ile Leu Met Leu Cys Thr Leu Ala Leu Trp Ala
1 5 10
aag tca gtc agt gct ggc tcc agc ttc ctc agc ccc tcc cag aaa cca 95
Lys Ser Val Ser Ala Gly Ser Ser Phe Leu Ser Pro Ser Gln Lys Pro
15 20 25
cag gta aga cag ggt aaa ggg aag ccc cct cga gtt ggt cgg cga gac 143
Gln Val Arg Gln Gly Lys Gly Lys Pro Pro Arg Val Gly Arg Arg Asp
30 35 40
att gag agc ttt gct gag ctg ttt gag ggt ccc ctt cac cag gaa gac 191
Ile Glu Ser Phe Ala Glu Leu Phe Glu Gly Pro Leu His Gln Glu Asp
45 50 55 60
aaa cac aat acg atc aag gct cct ttt gag atg ggc atc acc atg agt 239
Lys His Asn Thr Ile Lys Ala Pro Phe Glu Met Gly Ile Thr Met Ser
65 70 75
gag gag gag ttc cag gag tatggtgccg tgctgcagaa gatcctgcag 287
Glu Glu Glu Phe Gln Glu
80

actgtgtgaa catcgtttga attgtaaaag atgaataaaa taacactgct tcctt 453

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP00/04907

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18, A61P5/06, A61P19/08, A61K45/00, A61K48/00, G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18, A61P5/06, A61P19/08, A61K45/00, A61K48/00, G01N33/53

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
SwissProt/PIR/GeneSeq, Genbank/EMBL/DDBJ/GeneSeq, CA(STN), REGISTRY(STN), WPI (DIALOG), BIOSIS(DIALOG)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO, 98/42840, A1 (ZYMOGENETICS, INC.), 01 October, 1998 (01.10.98), p.19, pp.54-58 & AU, 9865769, A & NO, 9904614, A & EP, 975760, A1 & BR, 9808059, A & CN, 1254375, A	1-32,40-53
X	BLUET-PAJOT, M-T. et al., "Hypothalamic and hypophyseal regulation of growth hormone secretion", Cellular and Molecular Neurobiology (1998), Vol.18, No.1 pp.101-104, p.109	1,5,33-36, 39,54,56
P,X	KOJIMA, M. et al., Ghrelin is a growth-hormone-releasing acylated peptide from stomach", NATURE(Dec.1999), Vol.402, No.9, pp.656-660	1-36,39-54, 56
P,X	HOSODA, H. et al., "Purification and characterization of rat des-Gln^{14}-Ghrelin,a second endogenous ligand for the growth hormone secretagogue receptor", J. Biol. Chem. (MAY,2000), Vol.275, No.29, pp.21995-22000	1-36,39-54, 56
P,X	WO, 99/63088, A2 (GENENTECH, INC.),	1-32,40-53

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 October, 2000 (17.10.00)	24 October, 2000 (24.10.00)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP00/04907

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	09 December, 1999 (09.12.99), & AU, 9943286	

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP00/04907

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 37-39,55,57
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 37, 38, 55 and 57 pertain to methods for treatment of the human body by therapy and thus relate to a subject matter which this International Searching Authority is not required to search.

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

国際調査報告

国際出願番号　PCT／JP00／04907

A.　発明の属する分野の分類（国際特許分類（IPC））
Int Cl⁷ C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18, A61P5/06, A61P19/08, A61K45/00, A61K48/00, G01N33/53

B.　調査を行った分野
調査を行った最小限資料（国際特許分類（IPC））
Int Cl⁷ C07K14/47, C12N15/12, C12N1/21, C12P21/02, C07K16/18, A61K38/18, A61P5/06, A61P19/08, A61K45/00, A61K48/00, G01N33/53

最小限資料以外の資料で調査を行った分野に含まれるもの

国際調査で使用した電子データベース（データベースの名称、調査に使用した用語）
SwissProt/PIR/GeneSeq, Genbank/EMBL/DDBJ/GeneSeq, CA(STN), REGISTRY(STN), WPI(DIALOG), BIOSIS(DIALOG)

C.　関連すると認められる文献

引用文献のカテゴリー＊	引用文献名　及び一部の箇所が関連するときは、その関連する箇所の表示	関連する請求の範囲の番号
X	WO, 98/42840, A1 (ZYMOGENETICS, INC.) 1.10月.1998 (01.10.98) p.19, p54-58 &AU, 9865769, A &NO, 9904614, A &EP, 975760, A1 &BR, 9808059, A &CN, 1254375, A	1-32, 40-53
X	BLUET-PAJOT, M-T. et al. "Hypothalamic and hypophyseal regulation of growth hormone secretion", Cellular and Molecular Neurobiology (1998)第18巻, 第1号 p.101-104, 109	1, 5, 33-36, 39, 54, 56

☒ C欄の続きにも文献が列挙されている。　☐ パテントファミリーに関する別紙を参照。

＊ 引用文献のカテゴリー
「A」特に関連のある文献ではなく、一般的技術水準を示すもの
「E」国際出願日前の出願または特許であるが、国際出願日以後に公表されたもの
「L」優先権主張に疑義を提起する文献又は他の文献の発行日若しくは他の特別な理由を確立するために引用する文献（理由を付す）
「O」口頭による開示、使用、展示等に言及する文献
「P」国際出願日前で、かつ優先権の主張の基礎となる出願の日の後に公表された文献
「T」国際出願日又は優先日後に公表された文献であって出願と矛盾するものではなく、発明の原理又は理論の理解のために引用するもの
「X」特に関連のある文献であって、当該文献のみで発明の新規性又は進歩性がないと考えられるもの
「Y」特に関連のある文献であって、当該文献と他の1以上の文献との、当業者にとって自明である組合せによって進歩性がないと考えられるもの
「&」同一パテントファミリー文献

国際調査を完了した日	国際調査報告の発送日
17.10.00	24.10.00

国際調査機関の名称及びあて先	特許庁審査官（権限のある職員）		
日本国特許庁（ISA／JP） 郵便番号100-8915 東京都千代田区霞が関三丁目4番3号	六笠　紀子　印	4B	9735
	電話番号　03-3581-1101　内線　3448		

様式PCT／ISA／210（第2ページ）（1998年7月）

C（続き）．　関連すると認められる文献

引用文献のカテゴリー＊	引用文献名　及び一部の箇所が関連するときは、その関連する箇所の表示	関連する請求の範囲の番号
P, X	KOJIMA, M. et al. "Ghrelin is a growth-hormone-releasing acylated peptide from stomach", NATURE (Dec. 1999) 第402巻, 第9号 p. 656-660	1-36, 39-54, 56
P, X	HOSODA, H. et al. "Purification and characterization of rat des-Gln^{14}-Ghrelin, a second endogenous ligand for the growth hormone secretagogue receptor", J. Biol. Chem. (MAY, 2000) 第275巻, 第29号 p. 21995-22000	1-36, 39-54, 56
P, X	WO, 99/63088, A2 (GENENTECH, INC.) 9. 12月. 1999 (09. 12. 99) &AU, 9943286	1-32, 40-53

国際調査報告

国際出願番号 PCT／JP00／04907

第Ⅰ欄 請求の範囲の一部の調査ができないときの意見（第１ページの２の続き）

法第８条第３項（ＰＣＴ１７条(2)(a)）の規定により、この国際調査報告は次の理由により請求の範囲の一部について作成しなかった。

1. ☒ 請求の範囲 37,38,55,57 は、この国際調査機関が調査をすることを要しない対象に係るものである。
つまり、
請求の範囲３７、３８、５５及び５７は、人の身体の治療による処置方法であるから、この国際調査機関が調査をすることを要しない対象に係るものである。

2. ☐ 請求の範囲 _____ は、有意義な国際調査をすることができる程度まで所定の要件を満たしていない国際出願の部分に係るものである。つまり、

3. ☐ 請求の範囲 _____ は、従属請求の範囲であってＰＣＴ規則6.4(a)の第２文及び第３文の規定に従って記載されていない。

第Ⅱ欄 発明の単一性が欠如しているときの意見（第１ページの３の続き）

次に述べるようにこの国際出願に二以上の発明があるとこの国際調査機関は認めた。

1. ☐ 出願人が必要な追加調査手数料をすべて期間内に納付したので、この国際調査報告は、すべての調査可能な請求の範囲について作成した。

2. ☐ 追加調査手数料を要求するまでもなく、すべての調査可能な請求の範囲について調査することができたので、追加調査手数料の納付を求めなかった。

3. ☐ 出願人が必要な追加調査手数料を一部のみしか期間内に納付しなかったので、この国際調査報告は、手数料の納付のあった次の請求の範囲のみについて作成した。

4. ☐ 出願人が必要な追加調査手数料を期間内に納付しなかったので、この国際調査報告は、請求の範囲の最初に記載されている発明に係る次の請求の範囲について作成した。

追加調査手数料の異議の申立てに関する注意
☐ 追加調査手数料の納付と共に出願人から異議申立てがあった。
☐ 追加調査手数料の納付と共に出願人から異議申立てがなかった。